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FILE 'HOME' ENTERED AT 10:14:46 ON 01 AUG 2003

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 10:15:05 ON 01 AUG 2003

FILE 'EMBASE' ENTERED AT 10:15:05 ON 01 AUG 2003

FILE 'BIOSIS' ENTERED AT 10:15:05 ON 01 AUG 2003

FILE 'SCISEARCH' ENTERED AT 10:15:05 ON 01 AUG 2003

=> s mhc(W)class(W)ii
L1 36801 MHC(W) CLASS(W) II

=> s single(W)chain
L2 18463 SINGLE(W) CHAIN

=> s truncate or truncated or truncation
L3 233664 TRUNCATE OR TRUNCATED OR TRUNCATION

=> s transmembrane
L4 155056 TRANSMEMBRANE

=> s soluble
L5 454140 SOLUBLE

=> s l1 and l2
L6 61 L1 AND L2

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 28 DUP REM L6 (33 DUPLICATES REMOVED)

=> d ibib abs total

L7 ANSWER 1 OF 28 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003169133 MEDLINE
DOCUMENT NUMBER: 22573465 PubMed ID: 12686502
TITLE: A novel ***single*** ***chain*** I-A(b) molecule can stimulate and stain antigen-specific T cells.
AUTHOR: Thayer Wesley P; Dao Chinh T; Ignatowicz Leszek; Jensen Peter E
CORPORATE SOURCE: Department of Pathology and Laboratory of Medicine, Emory University School of Medicine, Atlanta, GA 30322, USA.
CONTRACT NUMBER: AI30554 (NIAID)
AI33614 (NIAID)
SOURCE: MOLECULAR IMMUNOLOGY, (2003 May) 39 (14) 861-70.

Journal code: 7905289. ISSN: 0161-5890.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTIC
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030416
Last Updated on STN: 20030619
Entered Medline: 20030618

AB Multimers of soluble major histocompatibility complex class I and II molecules have proven to be useful reagents in quantifying and following specific T cell populations. This study describes the design, generation, and characterization of a novel, ***single*** ***chain*** I-A(b) molecule which utilizes a unique linker derived from the murine invariant chain. A fragment of the invariant chain, residues 58-85, binds to a region proximal to the class II peptide binding groove and stabilizes occupancy of the class II invariant chain-associated peptide. We have utilized this fragment, replacing CLIP with the Ealpha peptide sequence, to lock the attached peptide into the class II binding groove. The ***single*** ***chain*** I-A(b) molecule was recognized by a panel of conformation-sensitive, I-A(b)-specific, monoclonal antibodies. Membrane-bound and soluble forms of the ***single*** ***chain*** I-A(b) stimulated an antigen-specific T cell hybridoma, and tetramers made from soluble monomers stained these cells. The unique features of this molecule may be useful in the design of recombinant T cell receptor ligands containing peptides with low affinity for MHC.

L7 ANSWER 2 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2002:204605 SCISEARCH
THE GENUINE ARTICLE: 524AR
TITLE: A ***single*** - ***chain*** class II MHC-IgG3 fusion protein inhibits autoimmune arthritis by induction of antigen-specific hyporesponsiveness
AUTHOR: Zuo L; Cullen C M; DeLay M L; Thornton S; Myers L K; Rosloniec E F; Boivin G P; Hirsch R (Reprint)
CORPORATE SOURCE: Childrens Hosp, Med Ctr, Div Rheumatol, Pav 2-129, 3333 Burnet Ave, Cincinnati, OH 45229 USA (Reprint); Childrens Hosp, Med Ctr, Div Rheumatol, Cincinnati, OH 45229 USA; Univ Cincinnati, Div Comparat Pathol, Cincinnati, OH 45229 USA; Univ Tennessee, Ctr Hlth Sci, Dept Pediat, Memphis, TN 38163 USA; Vet Affairs Med Ctr, Memphis, TN 38163 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF IMMUNOLOGY, (1 MAR 2002) Vol. 168, No. 5, pp. 2554-2559.
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 49
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB T cells play a central role in many autoimmune diseases. A method to specifically target the function of autoreactive T cell clones would avoid the global immunosuppression associated with current therapies. To develop a molecule capable of inhibiting autoreactive T cell responses in vivo, ***single*** - ***chain*** peptide-1-A-IgG3 fusion proteins were constructed and expressed in both mammalian and insect cells. The fusion proteins were designed with an IgG3 Fe moiety to make them divalent, allowing TCR cross-linking, while lacking FcR binding and costimulation. The fusion proteins stimulated T cell hybridomas in vitro in a peptide-specific, MHC-restricted manner but failed to do so in soluble form. In vivo administration of an I-A(q) fusion protein, containing an immunodominant collagen II peptide, significantly delayed the onset and

reduced the severity of collagen-induced arthritis in DBA/1 mice by induction of Ag-specific hyporesponsiveness. Such fusion proteins may be useful to study novel therapeutic approaches for T cell-mediated autoimmune diseases.

L7 ANSWER 3 OF 28 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002274204 MEDLINE
DOCUMENT NUMBER: 22008792 PubMed ID: 12014649
TITLE: T-cell immunotherapy for human MK-1-expressing tumors using a fusion protein of the superantigen SEA and anti-MK-1 scFv antibody.
AUTHOR: Ueno Aruto; Arakawa Fumiko; Abe Hironori; Matsumoto Hisanobu; Kudo Toshio; Asano Ryutaro; Tsumoto Kohei; Kumagai Izumi; Kuroki Motomu; Kuroki Masahide
CORPORATE SOURCE: Department of Biochemistry, Fukuoka University School of Medicine, Japan.
SOURCE: ANTICANCER RESEARCH, (2002 Mar-Apr) 22 (2A) 769-76. Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020517
Last Updated on STN: 20020628
Entered Medline: 20020627

AB BACKGROUND: The bacterial superantigen staphylococcal enterotoxin A (SEA) is an extremely potent activator of T lymphocytes when presented on major histocompatibility complex (***MHC***) ***class*** ***II*** molecules. To develop a tumor-specific superantigen for cancer therapy, we constructed a recombinant fusion protein of SEA and the ***single*** - ***chain*** variable fragment (scFv) of the FU-MK-1 antibody, which recognizes a glycoprotein antigen (termed MK-1 antigen) present on most carcinomas. MATERIALS AND METHODS: We employed recombinant DNA techniques to fuse recombinant mutant SEA to an scFv antibody derived from FU-MK-1 and the resulting fusion protein (SEA/FUscFv) was produced by a bacterial expression system, purified with a metal-affinity column, and characterized for its MK-1-binding specificity and its antitumor activity. RESULTS: The SEA/FUscFv fusion protein retained the reactivity with MK-1-expressing tumor cells, introduced a specific cytotoxicity of lymphokine-activated killer T-cells to the tumor cells, and consequently suppressed the tumor growth in a SCID mouse xenograft model. CONCLUSION: This genetically engineered SEA/FUscFv fusion protein may serve as a potentially useful immunotherapeutic reagent for human MK-1-expressing tumors.

L7 ANSWER 4 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:369099 BIOSIS
DOCUMENT NUMBER: PREV200200369099
TITLE: Cytotoxic T lymphocyte associated antigen-4 (CTLA-4) engagement has a long lasting effect on subsequent T cell responses.
AUTHOR(S): Engelhardt, John Joseph (1); Kuhns, Michael; Sullivan, Timothy; Allison, James P.
CORPORATE SOURCE: (1) Molecular and Cell Biology, University of California, 415 Life Science Addition, Berkeley, CA, 94720 USA
SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A711. http://www.fasebj.org/. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.
DOCUMENT TYPE: Conference

LANGUAGE: English

AB CTLA-4 provides an inhibitory signal for T cell activation when interacting with its ligands, B7.1 and B7.2, on antigen presenting cells(APCs). This inhibitory signal can function in primary and previously activated T cells. We have found that engagement of CTLA-4 in primary stimulations can have long lasting effects upon T cell responses to subsequent antigen encounter. Artificial APCs that express appropriate ***MHC*** ***class*** ***II*** molecules and membrane bound ***single*** ***chain*** antibodies (scFvs) against CTLA-4 and CD28 were used to specifically ligate either CD28, CTLA-4 or both CD28 and CTLA-4 during primary stimulations of TCR transgenic cells with their cognate peptide antigen. Upon restimulation with peptide-MHC bearing APCs expressing B7.2, rather than scFvs, cells that had CTLA-4 ligated in the primary stimulation were less responsive in secondary stimulations, based on proliferation and IFN-g secretion. These differences corresponded with different protein tyrosine phosphorylation patterns seen before and after secondary antigen encounter. These data suggest that CTLA-4 ligation, upon primary antigen encounter, affects T cell responses to future antigen encounter, and that there is a sustained biochemical basis for this effect.

L7 ANSWER 5 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

ACCESSION NUMBER: 2002:238712 SCISEARCH
THE GENUINE ARTICLE: 530NL

TITLE: Modeling the presentation of C3d-coated antigen by B lymphocytes: enhancement by CR1/2-BCR co-ligation is selective for the co-ligating antigen

AUTHOR: Prechl J; Baiu D C; Horvath A; Erdei A (Reprint)
CORPORATE SOURCE: Lorand Eotvos Univ, Dept Immunol, Pazmany Peter S 1-C, Budapest, Hungary (Reprint); Lorand Eotvos Univ, Dept Immunol, Budapest, Hungary; Hungarian Acad Sci, Res Grp, Budapest, Hungary; Ctr Immunol, Bucharest, Romania
COUNTRY OF AUTHOR: Hungary; Romania

SOURCE: INTERNATIONAL IMMUNOLOGY, (MAR 2002) Vol. 14, No. 3, pp. 241-247.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0953-8178.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 34

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have used a set of ***single*** - ***chain*** variable fragment antibodies (sc) genetically fused with an influenza hemagglutinin-derived peptide as a means to investigate the role of CR1 and CR2 in antigen presentation by B cells. When incubated with the B cell lymphoma 2130, peptide-containing sc specific for either CR1 or CR1/2 mediated activation of the hemagglutinin peptide-specific T cell line IP-12-7, as assessed by IL-2 production. Efficient presentation was dependent on the binding of the constructs to CR1/2, implying that receptor-mediated endocytosis is responsible for the effect. Cross-linkage of CR1/2 or CD19 by mAb did not increase the extent of T cell activation. However, when CR1/2 was co-ligated with the BCR-using either polyclonal goat anti-mouse IgG or recombinant protein LA-the antigen concentration required to activate T cells decreased by two orders of magnitude. Moreover, this enhancement was selective for the antigen included in these complexes and did not affect the presentation of a free peptide or of antigen bound to CR1/2 excluded from the complexes. These results suggest that B cells may bind various C3d-coated antigens at a time, but only the one which reacts with the BCR will be processed with high efficiency. This mechanism may ensure the specificity of cognate T cell help.

L7 ANSWER 6 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:6971 BIOSIS
DOCUMENT NUMBER: PREV200200006971
TITLE: MHC molecules and uses thereof.
AUTHOR(S): Rhode, Peter R.; Jiao, Jin-An (1); Burkhardt, Martin; Wong, Hing C.
CORPORATE SOURCE: (1) Fort Lauderdale, FL USA
ASSIGNEE: Sunol Molecular Corporation
PATENT INFORMATION: US 6309645 October 30, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 30, 2001) Vol. 1251, No. 5, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The present invention relates to novel complexes of major histocomability complex (MHC) molecules and uses of such complexes. In one aspect, the invention relates to loaded MHC complexes that include at least one MHC molecule with a peptide-binding groove and a presenting peptide non-covalently linked to the MHC protein. In another aspect, the invention features ***single*** ***chain*** ***MHC*** ***class*** ***II*** peptide fusion complexes with a presenting peptide covalently linked to the peptide binding grove of the complex. MHC complexes of the invention are useful for a variety of applications including: 1) in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, and 2) methods for suppressing or inducing an immune response in a mammal.

L7 ANSWER 7 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:499745 BIOSIS
DOCUMENT NUMBER: PREV200100499745
TITLE: Soluble MHC complexes and methods of use thereof.
AUTHOR(S): Rhode, Peter R.; Acevedo, Jorge (1); Burkhardt, Martin; Jiao, Jin-an; Wong, Hing C.
CORPORATE SOURCE: (1) Miami, FL USA
ASSIGNEE: Sunol Molecular Corporation
PATENT INFORMATION: US 6232445 May 15, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 15, 2001) Vol. 1246, No. 3, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The present invention relates to novel complexes of major histocompability complex (MHC) molecules and uses of such complexes. In one aspect, the invention relates to ***single*** ***chain*** ***MHC*** ***class*** ***II*** complexes that include a class II beta2 chain modification, e.g., deletion of essentially the entire class II beta2 chain. In another aspect, the invention features ***single*** ***chain*** ***MHC*** ***class*** ***II*** which comprise a immunoglobin constant chain or fragment. Further provided are polyspecific MHC complexes comprising at least one ***single*** ***chain*** ***MHC*** ***class*** ***II*** molecule. MHC complexes of the invention are useful for a variety of applications including: 1) in vitro screens for identification and isolation of peptides that modulate activity of selected T cells, including peptides that are T cell receptor antagonists and partial agonists, and 2) methods for suppressing or inducing an immune response in a mammal.

L7 ANSWER 8 OF 28 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001362548 MEDLINE
DOCUMENT NUMBER: 21316528 PubMed ID: 11319230
TITLE: Design, engineering, and production of human recombinant t

cell receptor ligands derived from human leukocyte antigen DR2.

AUTHOR: Chang[redacted] W; Mechling D E; Baching[redacted] H P; Burrows G G

CORPORATE SOURCE: Department of Neurology, Shriner's Hospital for Children, and Department of Biochemistry and Molecular Biology, Oregon Health Sciences University, Portland, Oregon 97201, USA.

CONTRACT NUMBER: AI43960 (NIAID)
ES10554 (NIEHS)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Jun 29) 276 (26) 24170-6.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200108

ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20030105
Entered Medline: 20010816

AB Major histocompatibility complex (***MHC***) ***class*** ***II*** molecules are membrane-anchored heterodimers on the surface of antigen-presenting cells that bind the T cell receptor, initiating a cascade of interactions that results in antigen-specific activation of clonal populations of T cells. Susceptibility to multiple sclerosis is associated with certain ***MHC*** ***class*** ***II*** haplotypes, including human leukocyte antigen (HLA) DR2. Two DRB chains, DRB5*0101 and DRB1*1501, are co-expressed in the HLA-DR2 haplotype, resulting in the formation of two functional cell surface heterodimers, HLA-DR2a (DRA*0101, DRB5*0101) and HLA-DR2b (DRA*0101, DRB1*1501). Both isotypes can present an immunodominant peptide of myelin basic protein (MBP-(84-102)) to MBP-specific T cells from multiple sclerosis patients. We have previously demonstrated that the peptide binding/T cell recognition domains of rat ***MHC*** ***class*** ***II*** (alpha1 and beta1 domains) could be expressed as a single exon for structural and functional characterization; Burrows, G. G., Chang, J. W., Bachinger, H.-P., Bourdette, D. N., Wegmann, K. W., Offner, H., and Vandenbark A. A. (1999) Protein Eng. 12, 771-778; Burrows, G. G., Adlard, K. L., Bebo, B. F., Jr., Chang, J. W., Tenditnyy, K., Vandenbark, A. A., and Offner, H. (2000) J. Immunol. 164, 6366-6371). ***Single*** - ***chain*** human recombinant T cell receptor ligands (RTLs) of approximately 200 amino acid residues derived from HLA-DR2b were designed using the same principles and have been produced in Escherichia coli with and without amino-terminal extensions containing antigenic peptides. Structural characterization using circular dichroism predicted that these molecules retained the antiparallel beta-sheet platform and antiparallel alpha-helices observed in the native HLA-DR2 heterodimer. The proteins exhibited a cooperative two-state thermal unfolding transition, and DR2-derived RTLs with a covalently linked MBP peptide (MBP-(85-99)) showed increased stability to thermal unfolding relative to the empty DR2-derived RTLs. These novel molecules represent a new class of small soluble ligands for modulating the behavior of T cells and provide a platform technology for developing potent and selective human diagnostic and therapeutic agents for treatment of autoimmune disease.

L7 ANSWER 9 OF 28 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2001195350 MEDLINE

DOCUMENT NUMBER: 21101944 PubMed ID: 11106664

TITLE: T Cell Receptor Binding to a pMHCII Ligand Is Kinetically Distinct from and Independent of CD4.

AUTHOR: Xiong Y; Kern P; Chang H; Reinherz E

CORPORATE SOURCE: Laboratory of Immunobiology, Dana-Farber Cancer Institute and Department of Medicine, Harvard Medical School, Boston,

Massachusetts 02115, USA.
CONTRACT NUMBER: AI19807 (NIAID)
AI43649 (NIAID)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Feb 23) 276 (8) 5659-67.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20030105
Entered Medline: 20010405

AB Immune recognition of pMHCII ligands by a helper T lymphocyte involves its antigen-specific T cell receptor (TCR) and CD4 coreceptor. We have characterized the binding of both molecules to the same pMHCII. The D10 alphabeta TCR heterodimer binds to conalbumin/I-A(k) with virtually identical kinetics and affinity as the ***single*** ***chain*** ValphaVbeta domain module (scD10) (Kd = 6-8 microm). The CD4 ectodomain does not alter either interaction. Moreover, CD4 alone demonstrates weak pMHCII binding (Kd = 200 microm), with no discernable affinity for the alphabeta TCR heterodimer. Hence, rather than providing a major contribution to binding energy, the critical role for the coreceptor in antigen-specific activation likely results from transient inducible recruitment of the CD4 cytoplasmic tail-associated lck tyrosine kinase to the pMHCII-ligated TCR complex.

L7 ANSWER 10 OF 28 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001248183 MEDLINE
DOCUMENT NUMBER: 21189417 PubMed ID: 11292343
TITLE: High affinity T cell receptors from yeast display libraries block T cell activation by superantigens.
AUTHOR: Kieke M C; Sundberg E; Shusta E V; Mariuzza R A; Wittrup K D; Kranz D M
CORPORATE SOURCE: Department of Biochemistry, University of Illinois, Urbana, IL, 61801, USA.
CONTRACT NUMBER: AI42937 (NIAID)
GM52801 (NIGMS)
GM55767 (NIGMS)
T32 GM07283 (NIGMS)
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (2001 Apr 13) 307 (5) 1305-15.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB The alphabeta T cell receptor (TCR) can be triggered by a class of ligands called superantigens. Enterotoxins secreted by bacteria act as superantigens by simultaneously binding to an ***MHC*** ***class*** ***II*** molecule on an antigen- presenting cell and to a TCR beta-chain, thereby causing activation of the T cell. The cross-reactivity of enterotoxins with different Vbeta regions can lead to stimulation of a large fraction of T cells. To understand the molecular details of TCR-enterotoxin interactions and to generate potential antagonists of these serious hyperimmune reactions, we engineered soluble TCR mutants with improved affinity for staphylococcal enterotoxin C3 (SEC3). A library of randomly mutated, ***single*** - ***chain***

TCRs (Vbeta-linker-Valpha) were expressed as fusions to the Aga2p protein on the surface of yeast cells. Mutants were selected by flow cytometric cell sorting with a fluorescent-labeled SEC3. Various mutations were identified, primarily in Vbeta residues that are located at the TCR:SEC3 interface. The combined mutations created a remodeled SEC3-binding surface and yielded a Vbeta domain with an affinity that was increased by 1000-fold (K(D)=7 nM). A soluble form of this Vbeta mutant was a potent inhibitor of SEC3-mediated T cell activity, suggesting that these engineered proteins may be useful as antagonists.

L7 ANSWER 11 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:825009 SCISEARCH
THE GENUINE ARTICLE: 480NH
TITLE: Specific immunotherapy of cancer in elderly patients
AUTHOR: Matzku S; Zoller M (Reprint)
CORPORATE SOURCE: German Canc Res Ctr, Dept Tumor Progress & Immune Def, Neuenheimer Feld 280, D-69120 Heidelberg, Germany (Reprint); German Canc Res Ctr, Dept Tumor Progress & Immune Def, D-69120 Heidelberg, Germany; Merck KGaA, Dept Oncol Biomed Res, Darmstadt, Germany; Univ Karlsruhe, Dept Appl Genet, Karlsruhe, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: DRUGS & AGING, (1 SEP 2001) Vol. 18, No. 9, pp. 639-664. Publisher: ADIS INTERNATIONAL LTD, 41 CENTORIAN DR, PRIVATE BAG 65901, MAIRANGI BAY, AUCKLAND 10, NEW ZEALAND. ISSN: 1170-229X.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 370
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The concept of immunotherapy of cancer is more than a century old, but only recently have molecularly defined therapeutic approaches been developed. In this review, we focus on the most promising approach, active therapeutic vaccination.

The identification of tumour antigens can now be accelerated by methods allowing the amplification of gene products selectively or preferentially transcribed in the tumour. However, determining the potential immunogenicity of such gene products remains a demanding task, since major histocompatibility complex (MHC) restriction of T cells implies that for any newly defined antigen, immunogenicity will have to be defined for any individual MHC haplotype. Tumour-derived peptides elated from MHC molecules of tumour tissue are also a promising source of antigen.

Tumour antigens are mostly of weak immunogenicity, because the vast majority are tumour-associated differentiation antigens already 'seen' by the patient's immune system. Effective therapeutic vaccination will thus require adjuvant support, possibly by new approaches to immunomodulation such as bispecific antibodies or antibody-cytokine fusion proteins. Tumour-specific antigens, which could be a more potent target for immunotherapy, mostly arise by point mutations and have the disadvantage of being not only tumour-specific, but also individual-specific. Therapeutic vaccination will probably focus on defined antigens offered as protein, peptide or nucleic acid. Irrespective of the form in which the antigen is applied, emphasis will be given to the activation of dendritic cells as professional antigen presenters. Dendritic cells may be loaded in vitro with antigen, or, alternatively, initiation of an immune response may be approached in vivo by vaccination with RNA or DNA, given as such or packed into attenuated bacteria.

The importance of activation of T helper cells has only recently been taken into account in cancer vaccination. Activation of cytotoxic T cells is facilitated by the provision of T helper cell-derived cytokines. T helper cell-dependent recruitment of elements of non-adaptive defence, such as leucocytes, natural killer cells and monocytes, is of particular

importance when the tumour has lost MHC class I expression.
Barriers to successful therapeutic vaccination include: (i) the escape mechanisms developed by tumour cells in response to immune attack; (ii) tolerance or anergy of the evoked immune response; (iii) the theoretical possibility of provoking an autoimmune reaction by vaccination against tumour-associated antigens; and (iv) the advanced age of many patients, implying reduced responsiveness of the senescent immune system.

L7 ANSWER 12 OF 28 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001086806 MEDLINE
DOCUMENT NUMBER: 20558264 PubMed ID: 11106438
TITLE: Expression and characterization of truncated forms of humanized L243 IgG1. Architectural features can influence synthesis of its oligosaccharide chains and affect superoxide production triggered through human Fcgamma receptor I.
AUTHOR: Lund J; Takahashi N; Popplewell A; Goodall M; Pound J D; Tyler R; King D J; Jefferis R
CORPORATE SOURCE: Department of Immunology, The Medical School, Birmingham, UK.. J.Lund@bham.ac.uk
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (2000 Dec) 267 (24) 7246-57.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118

AB The properties of IgG and its subcomponents are being exploited to generate new therapeutics with selected biological activities. In this study, a series of truncated, humanized IgG1 antibodies was expressed in Chinese hamster ovary cells, to evaluate the contribution of structural components to glycosylation and function. The series includes L243 IgG1 (alpha- ***MHC*** ***Class*** ***II***) lacking a CH3 domain pair (DeltaCH3-IgG1), ***single*** - ***chain*** Fv fusion proteins with Fc or a hinge-CH2 domain, Fc with/out a hinge, and a single CH2 domain. Glycosylation of IgG Fc is important for recognition by effector ligands such as Fcgamma receptors. HPLC analysis of released and pyridylaminated oligosaccharides indicates that intact IgG1 and scFvFc antibodies are galactosylated and sialylated to levels similar to those observed previously for normal human IgG1. The truncated forms express increased levels of digalactosylated (30-83%) or sialylated (9-21%) oligosaccharide chains with the highest levels observed for the single CH2 domain. These data show which architectural components influence IgG glycosylation processing and that the (CH3)2 pair is particularly influential. When ***MHC*** ***Class*** ***II*** bearing (JY) cells were sensitized with L243 DeltaCH3-IgG1, scFvFc, or scFvhCH2 they elicited superoxide production, from U937 cells, at levels of 35-45% relative to that obtained for intact L243 IgG1 (100%). Mild reduction and alkylation of the hinge disulphide bonds of scFvhCH2 greatly decreased its capacity to trigger superoxide production. Thus, the L243 scFvhCH2 homo-dimer constitutes the minimal truncated form that binds the ***MHC*** ***Class*** ***II*** antigen and triggers superoxide production through FcgammaRI.

L7 ANSWER 13 OF 28 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000302788 MEDLINE
DOCUMENT NUMBER: 20302788 PubMed ID: 10843691
TITLE: Regulation of encephalitogenic T cells with recombinant TCR ligands.

AUTHOR: Burrows G G; Adlard K L; Bebo B F Jr; Chang J W; Tenditnyy K; Vandenbark A A; Offner H

CORPORATE SOURCE: Department of Neurology, Biochemistry and Molecular Biology, and Molecular Microbiology and Immunology, Oregon Health Sciences University, Portland 97201, USA.. ggb@ohsu.edu

SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Jun 15) 164 (12) 6366-71. Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200007

ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000720

AB We have previously described recombinant ***MHC*** ***class*** ***II*** beta1 and alpha1 domains loaded with free antigenic peptides with potent inhibitory activity on encephalitogenic T cells. We have now produced ***single*** - ***chain*** constructs in which the peptide Ag is genetically encoded within the same exon as the linked beta1 and alpha1 domains, overcoming the problem of displacement of peptide Ag from the peptide binding cleft. We here describe clinical effects of recombinant TCR ligands (RTLs) comprised of the rat RT1.B beta1alpha1 domains covalently linked to the 72-89 peptide of guinea pig myelin basic protein (RTL-201), to the corresponding 72-89 peptide from rat myelin basic protein (RTL-200), or to cardiac myosin peptide CM-2 (RTL-203). Only RTL-201 possessed the ability to prevent and treat active or passive experimental autoimmune encephalomyelitis. Amelioration of experimental autoimmune encephalomyelitis was associated with a selective inhibition of proliferation response and cytokine production by Ag-stimulated lymph node T cells and a drastic reduction in the number of encephalitogenic and recruited inflammatory cells infiltrating the CNS. The exquisitely selective inhibition could be observed between molecules that differ by a single methyl group (the single amino acid residue difference between RTL-200 (threonine) and RTL-201 (serine) at position 80 of the myelin basic protein peptide). These novel RTLs provide a platform for developing potent and selective human diagnostic and therapeutic agents for treatment of autoimmune disease.

L7 ANSWER 14 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

ACCESSION NUMBER: 2000:690374 SCISEARCH

THE GENUINE ARTICLE: 351FK

TITLE: Modulation of the peptide-binding specificity of a ***single*** - ***chain*** class II major histocompatibility complex

AUTHOR: Kim S T; Byun S M (Reprint)

CORPORATE SOURCE: KOREA ADV INST SCI & TECHNOL, DEPT BIOL SCI, 373-1 KUSUNG DONG, YUSUNG GU, TAEJON 305701, SOUTH KOREA (Reprint); KOREA ADV INST SCI & TECHNOL, DEPT BIOL SCI, TAEJON 305701, SOUTH KOREA

COUNTRY OF AUTHOR: SOUTH KOREA

SOURCE: JOURNAL OF BIOCHEMISTRY, (SEP 2000) Vol. 128, No. 3, pp. 449-454.
Publisher: JAPANESE BIOCHEMICAL SOC, ISHIKAWA BLDG-3F, 25-16 HONGO-5-CHOME, BUNKYO-KU, TOKYO 113, JAPAN.
ISSN: 0021-924X.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 35

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We designed and expressed a ***single*** - ***chain*** class II

major histocompatibility complex molecule capable of forming a stable complex with an antigenic peptide. The peptide-binding preference of the ***single*** - ***chain*** (sc) human leukocyte antigen derived from DRB5*0101 (DR51) was determined to be similar to that of the authentic one, which requires a bulky hydrophobic residue at position-1 (P1) as a primary anchor. For modulation of the peptide-binding affinity, we modified binding pocket 1 of sc DR51 by site-directed mutagenesis, The relative binding affinity of the engineered sc DR51 for several P1-substituted peptides was measured by competition assaying with a fluorescence labeled peptide. The sc DR51 molecule showed high affinity to the self-peptide derived from myelin basic protein, 87-98 with Phe as the P1 residue (F90F). While reduction of pocket 1 volume (beta G86V) decreased the affinity of F90F, it rather increased the affinity of the Ala-substituted peptide as to the P1 residue (F90A), Through more extensive engineering in the peptide-binding groove of the sc DR51 molecule, it is expected that we can construct sc DR51 variants with various peptide ligand motifs.

L7 ANSWER 15 OF 28 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2000242816 EMBASE
TITLE: Study of adoptive immunotherapy for bile duct carcinoma using SEA-scFv fusion protein.
AUTHOR: Takemura S.-I.; Kodama H.; Shinoda M.; Imai K.; Kudo T.
CORPORATE SOURCE: Dr. T. Kudo, Cell Rsrc. Ctr. for Biomedical Res., Inst. of Development, Aging/Cancer, Tohoku University, 4-1 Seiryo-cho, Aoba-ku, Sendai 9800872, Japan
SOURCE: Biotherapy, (2000) 14/5 (429-431).
Refs: 3
ISSN: 0914-2223 CODEN: BITPE
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB SEA is a superantigen derived from bacteria. It binds MHC crass II molecules and activates T cells expressing particular T-cell receptor (TCR) V.beta. elements. However, wild type SEA (SEA wt) might cause side effects such as septic shock in patients because of the nonspecific binding of SEA to ***MHC*** ***class*** ***II*** positive tissues. In order to reduce its affinity with ***MHC*** ***class*** ***II*** molecules, we have generated a mutated SEA (SEA D227A) through genetic engineering. Furthermore, we constructed and expressed two kinds of SEA- MUSE11 ***single*** ***chain*** Fv fusion proteins; namely, SEA wt-MUSE11 sCFv and SEA D227A-MUSE11 scFv, in a bacterial expression system. These fusion proteins showed specific tumor growth inhibition for the MUC1 positive bile duct carcinoma cell line TFK-1, and had equal functions to SEA-IgG. SEA D227A-scFv in particular, which has a lower affinity with ***MHC*** ***class*** ***II*** molecules and sufficient potential for T cell activation, might cause fewer side effects than SEA wt-scFv when administered to patients.

L7 ANSWER 16 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2000:908631 SCISEARCH
THE GENUINE ARTICLE: 377CF
TITLE: Survey of the 1999 surface plasmon resonance biosensor literature
AUTHOR: Rich R L; Myszka D G (Reprint)
CORPORATE SOURCE: UNIV UTAH, SCH MED, CTR BIOMOL INTERACT ANAL, NO 4A417, 50 N MED DR, SALT LAKE CITY, UT 84132 (Reprint); UNIV UTAH, SCH MED, CTR BIOMOL INTERACT ANAL, SALT LAKE CITY, UT

84132
COUNTRY OF AUTHOR: USA
SOURCE: JOUR[redacted]L OF MOLECULAR RECOGNITIO[redacted] (NOV-DEC 2000) Vol. 13, No. 6, pp. 388-407.
Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER, W SUSSEX PO19 1UD, ENGLAND.
ISSN: 0952-3499.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 506

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The application of surface plasmon resonance biosensors in life sciences and pharmaceutical research continues to increase. This review provides a comprehensive list of the commercial 1999 SPR biosensor literature and highlights emerging applications that are of general interest to users of the technology. Given the variability in the quality of published biosensor data, we present some general guidelines to help increase confidence in the results reported from biosensor analyses.

L7 ANSWER 17 OF 28 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1999436459 MEDLINE
DOCUMENT NUMBER: 99436459 PubMed ID: 10506287
TITLE: Design, engineering and production of functional ***single*** - ***chain*** T cell receptor ligands.
AUTHOR: Burrows G G; Chang J W; Bachinger H P; Bourdette D N; Offner H; Vandenbark A A
CORPORATE SOURCE: Department of Neurology, Department of Biochemistry and Molecular Biology and Department of Molecular Microbiology and Immunology, Oregon Health Sciences University, Portland, OR 97201, USA.
SOURCE: PROTEIN ENGINEERING, (1999 Sep) 12 (9) 771-8.
Journal code: 8801484. ISSN: 0269-2139.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000127

AB Major histocompatibility complex (***MHC***) ***class*** ***II*** molecules are membrane-anchored heterodimers on the surface of antigen presenting cells (APCs) that bind the T cell receptor, initiating a cascade of interactions that results in antigen-specific activation of clonal populations of T cells. The peptide binding/T cell recognition domains of rat ***MHC*** ***class*** ***II*** (alpha-1 and beta-1 domains) were expressed as a single exon for structural and functional characterization. These recombinant ***single*** - ***chain*** T cell receptor ligands (termed 'beta1alpha1' molecules) of approximately 200 amino acid residues were designed using the structural backbone of ***MHC*** ***class*** ***II*** molecules as template, and have been produced in Escherichia coli with and without N-terminal extensions containing antigenic peptides. Structural characterization using circular dichroism predicted that these molecules retained the antiparallel beta-sheet platform and antiparallel alpha-helices observed in the native ***MHC*** ***class*** ***II*** heterodimer. The proteins exhibited a cooperative two-state thermal folding-unfolding transition. Beta1alpha1 molecules with a covalently linked MBP-72-89 peptide showed increased stability to thermal unfolding relative to the empty beta1alpha1 molecules. This new class of small soluble polypeptide provides a template for designing and refining

human homologues useful in detecting and regulating pathogenic T cells.

L7 ANSWER 18 OF 28 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1999287109 MEDLINE
DOCUMENT NUMBER: 99287109 PubMed ID: 10360364
TITLE: Structure, specificity and CDR mobility of a class II restricted ***single*** - ***chain*** T-cell receptor.
AUTHOR: Hare B J; Wyss D F; Osburne M S; Kern P S; Reinherz E L; Wagner G
CORPORATE SOURCE: Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, Massachusetts 02115, USA.
SOURCE: NATURE STRUCTURAL BIOLOGY, (1999 Jun) 6 (6) 574-81.
Journal code: 9421566. ISSN: 1072-8368.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1BWM
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990712
Last Updated on STN: 19990712
Entered Medline: 19990623

AB Using NMR spectroscopy, we determined the solution structure of a ***single*** - ***chain*** T-cell receptor (scTCR) derived from the major histocompatibility complex (***MHC***) ***class*** ***II*** -restricted D10 TCR. The conformations of complementarity-determining regions (CDRs) 3beta and 1alpha and surface properties of 2alpha are different from those of related class I-restricted TCRs. We infer a conserved orientation for TCR V(alpha) domains in complexes with both class I and II MHC-peptide ligands, which implies that small structural variations in V(alpha) confer MHC class preference. High mobility of CDR3 residues relative to other CDR or framework residues (picosecond time scale) provides insight into immune recognition and selection mechanisms.

L7 ANSWER 19 OF 28 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 1999167366 MEDLINE
DOCUMENT NUMBER: 99167366 PubMed ID: 10066451
TITLE: SEA-scFv as a bifunctional antibody: construction of a bacterial expression system and its functional analysis.
COMMENT: Erratum in: Biochem Biophys Res Commun 1999 May 27;259(1):230
AUTHOR: Sakurai N; Kudo T; Suzuki M; Tsumoto K; Takemura S; Kodama H; Ebara S; Teramae A; Katayose Y; Shinoda M; Kurokawa T; Hinoda Y; Imai K; Matsuno S; Kumagai I
CORPORATE SOURCE: Tohoku University School of Medicine, Tohoku University, Sendai, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1999 Mar 5) 256 (1) 223-30.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 20000303
Entered Medline: 19990413

AB A SEA-antibody ***single*** ***chain*** Fv (SEA-scFv) fusion protein was produced by bacterial expression system in this study. SEA-scFv has both staphylococcal enterotoxin A (SEA) effects and antibody

activity directed at the epithelial mucin core protein MUC1, a cancer associated antigen. It was expressed mostly in the cytoplasm as an insoluble form. The gene product was solubilized by guanidine hydrochloride, refolded by conventional dilution method, and purified using metal-chelating chromatography. The resulting SEA-scFv fusion protein preparation was found to react with MUC1 and ***MHC*** ***class*** ***II*** antigens and had the ability to enhance cytotoxicity of lymphokine activated killer cells with a T cell phenotype against a human bile duct carcinoma cell line, TFK-1, expressing MUC1. This genetically engineered SEA-scFv fusion protein promises to be an important reagent for cancer immunotherapy.

L7 ANSWER 20 OF 28 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:528458 BIOSIS
DOCUMENT NUMBER: PREV199900528458
TITLE: Inhibition of collagen induced arthritis in mice with a ***single*** ***chain*** CII-IAq-IgG3 fusion protein
AUTHOR(S): Zuo, Li (1); Myers, Linda K.; Rosloniec, Edward F.; DeLay, Monica L.; Hirsch, Raphael
CORPORATE SOURCE: (1) Cincinnati, OH USA
SOURCE: Arthritis & Rheumatism, (Sept., 1999) Vol. 42, No. 9 SUPPL., pp. S125.
Meeting Info.: 63rd Annual Scientific Meeting of the American College of Rheumatology and the 34th Annual Scientific Meeting of the Association of Rheumatology Health Professionals Boston, Massachusetts, USA November 13-17, 1999
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 21 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 1999:774501 SCISEARCH
THE GENUINE ARTICLE: 243GF
TITLE: Cancer therapy: New concepts on active immunization
AUTHOR: Zoller M (Reprint); Matzku S
CORPORATE SOURCE: GERMAN CANC RES CTR, DEPT TUMOR PROGRESS & IMMUNE DEF, NEUENHEIMER FELD 280, D-69120 HEIDELBERG, GERMANY (Reprint); UNIV KARLSRUHE, DEPT APPL GENET, KARLSRUHE, GERMANY; MERCK KGA, DEPT IMMUNOL & ONCOL, PRECLIN PHARMA RES, DARMSTADT, GERMANY; GERMAN CANC RES CTR, DEPT TUMOR PROGRESS & IMMUNE DEF, D-69120 HEIDELBERG, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: IMMUNOBIOLOGY, (SEP 1999) Vol. 201, No. 1, pp. 1-21.
Publisher: GUSTAV FISCHER VERLAG, VILLENGANG 2, D-07745 JENA, GERMANY.
ISSN: 0171-2985.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 239
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB There is increasing evidence that tumors express putative target molecules for a therapeutic immune reaction. Yet, tumor cells lack the prerequisites for appropriate antigen presentation and - hence - the immune system does not respond. This difficulty can probably be circumvented when tumor antigens are processed by conventional antigen presenting cells. Thus, the identification of immunogenic tumor-associated antigens may allow new modes of vaccination with the hope of adding a fourth and hopefully powerful weapon to surgery, radiation and chemotherapy in the fight against cancer.

L7 ANSWER 22 OF 28 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 1999049826 MEDLINE
DOCUMENT NUMBER: 99049826 PubMed ID: 9834080
TITLE: Two-domain ***MHC*** ***class*** ***II*** molecules form stable complexes with myelin basic protein 69-89 peptide that detect and inhibit rat encephalitogenic T cells and treat experimental autoimmune encephalomyelitis.
AUTHOR: Burrows G G; Bebo B F Jr; Adlard K L; Vandenbark A A; Offner H
CORPORATE SOURCE: Veterans Affairs Medical Center, Department of Neurology, Oregon Health Sciences University, Portland 97201, USA.. ggb@ohsu.edu
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Dec 1) 161 (11) 5987-96. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19981221

AB We designed and expressed in bacteria a ***single*** - ***chain*** two-domain ***MHC*** ***class*** ***II*** molecule capable of binding and forming stable complexes with antigenic peptide. The prototype "beta1alpha1" molecule included the beta1 domain of the rat RT1.B class II molecule covalently linked to the amino terminus of the alpha1 domain. In association with the encephalitogenic myelin basic protein (MBP) 69-89 peptide recognized by Lewis rat T cells, the beta1alpha1/MBP-69-89 complex specifically labeled and inhibited activation of MBP-69-89 reactive T cells in an IL-2-reversible manner. Moreover, this complex both suppressed and treated clinical signs of experimental autoimmune encephalomyelitis and inhibited delayed-type hypersensitivity reactions and lymphocyte proliferation in an Ag-specific manner. These data indicate that the beta1alpha1/MBP-69-89 complex functions as a simplified natural TCR ligand with potent inhibitory activity that does not require additional signaling from the beta2 and alpha2 domains. This new class of small soluble polypeptide may provide a template for designing human homologues useful in detecting and regulating potentially autopathogenic T cells.

L7 ANSWER 23 OF 28 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 97439473 MEDLINE
DOCUMENT NUMBER: 97439473 PubMed ID: 9295029
TITLE: A recombinant ***single*** - ***chain*** human class II MHC molecule (HLA-DR1) as a covalently linked heterotrimer of alpha chain, beta chain, and antigenic peptide, with immunogenicity in vitro and reduced affinity for bacterial superantigens.
AUTHOR: Zhu X; Bavari S; Ulrich R; Sadegh-Nasseri S; Ferrone S; McHugh L; Mage M
CORPORATE SOURCE: Laboratory of Biochemistry, DCBDC, NCI, NIH, Bethesda, MD 20892, USA.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Aug) 27 (8) 1933-41. Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971013
Last Updated on STN: 19971013

Entered Medline: 19970930

AB Major histocompatibility complex (***MHC***) ***class*** ***II*** molecules bind to numerous peptides and display these on the cell surface for T cell recognition. In a given immune response, receptors on T cells recognize antigenic peptides that are a minor population of ***MHC*** ***class*** ***II*** -bound peptides. To control which peptides are presented to T cells, it may be desirable to use recombinant MHC molecules with covalently bound antigenic peptides. To study T cell responses to such homogeneous peptide-MHC complexes, we engineered an HLA-DR1 cDNA coding for influenza hemagglutinin, influenza matrix, or HIV p24 gag peptides covalently attached via a peptide spacer to the N terminus of the DR1 beta chain. Co-transfection with DR alpha cDNA into mouse L cells resulted in surface expression of HLA-DR1 molecules that reacted with monoclonal antibodies (mAb) specific for correctly folded HLA-DR epitopes. This suggested that the spacer and peptide did not alter expression or folding of the molecule. We then engineered an additional peptide spacer between the C terminus of a truncated beta chain (without transmembrane or cytoplasmic domains) and the N terminus of full-length DR alpha chain. Transfection of this cDNA into mouse L cells resulted in surface expression of the entire covalently linked heterotrimer of peptide, beta chain, and alpha chain with the expected molecular mass of approximately 66 kDa. These ***single*** - ***chain*** HLA-DR1 molecules reacted with mAb specific for correctly folded HLA-DR epitopes, and identified one mAb with [MHC + peptide] specificity. Affinity-purified soluble secreted ***single*** - ***chain*** molecules with truncated alpha chain moved in electrophoresis as compact class II MHC dimers. Cell surface two-chain or ***single*** - ***chain*** HLA-DR1 molecules with a covalent HA peptide stimulated HLA-DR1-restricted HA-specific T cells. They were immunogenic in vitro for peripheral blood mononuclear cells. The two-chain and ***single*** - ***chain*** HLA-DR1 molecules with covalent HA peptide had reduced binding for the bacterial superantigens staphylococcal enterotoxin A and B and almost no binding for toxic shock syndrome toxin-1. The unique properties of these engineered HLA-DR1 molecules may facilitate our understanding of the complex nature of antigen recognition and aid in the development of novel vaccines with reduced superantigen binding.

L7 ANSWER 24 OF 28 MEDLINE on STN DUPLICATE 13

ACCESSION NUMBER: 97098715 MEDLINE
DOCUMENT NUMBER: 97098715 PubMed ID: 8943392
TITLE: ***Single*** - ***chain*** ***MHC*** ***class*** ***II*** molecules induce T cell activation and apoptosis.
AUTHOR: Rhode P R; Burkhardt M; Jiao J; Siddiqui A H; Huang G P; Wong H C
CORPORATE SOURCE: Sunol Molecular Corporation, Miami, FL 33172, USA.
SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Dec 1) 157 (11) 4885-91. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961227

AB ***MHC*** ***class*** ***II*** /peptide complexes displayed on the surface of APCs play a pivotal role in initiating specific T cell responses. Evidence is presented here that components of this heterotrimeric complex can be genetically linked into a single polypeptide chain. Soluble ***single*** - ***chain*** (sc) murine class II IA(d) molecules with and without covalently attached peptides were

produced in a recombinant baculovirus-insect cell expression system. Correct conformation of these molecules was verified based on 1) reactivity to Abs directed against conformational epitopes in IA(d) and 2) peptide-specific recognition of the IA(d)/peptide complexes by T cells. Both sc class II molecules loaded the appropriate peptides and sc class II/peptide fusions were effective in stimulating T cell responses, including cytokine release and apoptosis. Mammalian cells were also found to be capable of expressing functional sc class II molecules on their cell surfaces. The findings reported here open up the possibility of producing large amounts of stable sc class II/peptide fusion molecules for structural characterization and immunotherapeutic applications.

L7 ANSWER 25 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 92:252796 SCISEARCH
THE GENUINE ARTICLE: HN012
TITLE: MOLECULAR-COMPONENTS OF T-CELL RECOGNITION
AUTHOR: JORGENSEN J L (Reprint); REAY P A; EHRICH E W; DAVIS M M
CORPORATE SOURCE: STANFORD UNIV, DEPT MICROBIOL & IMMUNOL, STANFORD, CA, 94305 (Reprint); STANFORD UNIV, HOWARD HUGHES MED INST, STANFORD, CA, 94305
COUNTRY OF AUTHOR: USA
SOURCE: ANNUAL REVIEW OF IMMUNOLOGY, (1992) Vol. 10, pp. 835-873. ISSN: 0732-0582.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 176

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We review recent data that increase our understanding of the ternary complex of the T cell receptor (TCR), antigenic peptides, and molecules of the major histocompatibility complex (MHC). Studies using synthetic peptide analogs for T-cell antigens have identified peptide residues that appear to interact with the MHC molecule and/or the TCR. The logical extension of these studies, using a complete replacement set of peptide analogues for a model peptide antigen, has more precisely defined the biochemical character of putative MHC and TCR contact residues, and indicated that the TCR is highly sensitive to subtle changes in peptide conformation. Insight into the binding site for peptide on the TCR has recently come from variant peptide immunization of TCR ***single*** - ***chain*** transgenic mice. These experiments indicate that residues encoded by the V(D)J junctions of both TCR chains contact peptide directly. TCR-MHC contacts have also been studied, using in vitro-mutagenized MHC molecules, particularly those altered at residues predicted to point "up," toward the TCR. These studies reveal that TCR-MHC contacts appear to be quite flexible, and vary between even closely related TCRs. A measure of the affinity of TCR for peptide/MHC complexes has come from competition experiments using soluble MHC complexed with specific peptides. This affinity, with a K(D) of 5 x 10(-5) M, is several orders of magnitude lower than that of most antibodies for their protein antigens and suggests that the sequence of events leading to T-cell activation begins with antigen-independent adhesion.

L7 ANSWER 26 OF 28 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 93056563 MEDLINE
DOCUMENT NUMBER: 93056563 PubMed ID: 1385534
TITLE: Preparative-scale purification and characterization of ***MHC*** ***class*** ***II*** monomers.
AUTHOR: Passmore D; Kopa D; Nag B
CORPORATE SOURCE: Anergen Inc., Redwood City, CA 94063.
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1992 Nov 5) 155 (2) 193-200.
Journal code: 1305440. ISSN: 0022-1759.

PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Engli
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19960129
Entered Medline: 19921209

AB The ***MHC*** ***class*** ***II*** molecule is a heterodimeric glycoprotein consisting of one alpha and one beta polypeptide chain of almost identical molecular size. Recently it has been shown by others, and confirmed in our laboratory, that isolated monomers of murine MHC II molecules are capable of binding antigenic peptides like the alpha/beta intact heterodimer. In addition, preliminary results from our laboratory indicate that isolated ***single*** ***chain*** -peptide complexes of murine ***MHC*** ***class*** ***II*** molecules are capable of stimulating cloned T cells in an antigen specific manner. These results prompted us to isolate relatively large quantities of individual alpha and beta subunits of MHC II molecules for further in vitro and in vivo studies. Isolation of alpha and beta monomers proved to be difficult using conventional chromatographic methods. In this report we describe micro-preparative and preparative continuous flow electrophoresis methods by which milligram quantities of MHC II subunits can be purified. An optimal condition for the dissociation of heterodimeric MHC II into alpha and beta monomers was identified, and separation of human HLA DR2 and murine IAs monomers was accomplished. Both methods offer the resolving power of gel electrophoresis with the convenience of continuous sample elution. Purified MHC II subunits obtained by these methods were tested for their ability to bind antigenic peptides. Results presented in this study indicate that monomeric subunits of both human HLA-DR2 and murine IAs are equally active in specific binding of antigenic peptides like the native heterodimer.

L7 ANSWER 27 OF 28 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 88014331 MEDLINE
DOCUMENT NUMBER: 88014331 PubMed ID: 3309687
TITLE: Supplementary characteristics of anti- ***MHC*** ***class*** ***II*** monoclonal antibodies elicited by an ALL cell line: immunofluorescence cytofluorometry, C-dependent cytotoxicity, two-dimensional analysis of antigen.
AUTHOR: Chorvath B; Duraj J; Sedlak J; Pleskova I; Munozova H; Buc M
CORPORATE SOURCE: Cancer Research Institute, Slovak Academy of Sciences, Bratislava, Czechoslovakia.
SOURCE: NEOPLASMA, (1987) 34 (4) 417-25.
Journal code: 0377266. ISSN: 0028-2685.
PUB. COUNTRY: Czechoslovakia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198710
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19871027

AB Monoclonal antibodies directed to ***MHC*** ***class*** ***II*** antigen(s), elicited by a non-T, non-B ALL cell line, were characterized by immunofluorescence flow cytofluorometry and ELISA immunofiltration measurements of their immunoreactivity with selected neoplastic hemopoietic cell lines, determination of their complement-dependent cytotoxic activity against isolated peripheral blood B and T lymphocytes and by two-dimensional electrophoretic analysis (isoelectric focusing, SDS-PAGE) of radiolabeled, immunoprecipitated by these antibodies cell

surface antigens. Patterns of these immunological reactivities, as well as two-dimensional radioimmunoprecipitation patterns (acidic heavy chain p35 and basic light chain p30) of antigens recognized by these antibodies confirm their anti- ***MHC*** ***class*** ***II*** specificity. One of these antibodies (braFB6; IgG2b) displayed identical pattern of expression on cell lines and cell types as the typical anti- ***MHC*** ***class*** ***II*** antibodies, but immunoprecipitated only a ***single*** ***chain*** p30 radioiodinated cell surface protein (with two-dimensional pattern close to the beta-chain of ***MHC*** ***class*** ***II*** DR antigen). These properties indicate the ability of braFB6 monoclonal antibody to recognize a nonpolymorphic determinant of DP- ***MHC*** ***class*** ***II*** antigen.

L7 ANSWER 28 OF 28 MEDLINE on STN
ACCESSION NUMBER: 83163003 MEDLINE
DOCUMENT NUMBER: 83163003 PubMed ID: 6187884
TITLE: In vitro correlate for a clonal deletion mechanism of immune response gene-controlled nonresponsiveness.
AUTHOR: Ishii N; Nagy Z A; Klein J
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1983 Mar 1) 157 (3) 998-1005.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198305
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19900318
Entered Medline: 19830505

AB We used T cell-antigen-presenting cell (APC) combinations from two pairs of recombinant mouse strains, B10.A(4R)-B10.A(2R) and B10.S(7R)-B10.S(9R) (abbreviated 4R, 2R, 7R, 9R, respectively), which differ from each other only in the nonexpression vs. expression of cell-surface E molecules, to study the mechanism of the Ir gene-controlled (E-restricted) response to the terpolymer poly(glu51lys34tyr15) (GLT). No response to GLT occurred when the APC were from E-nonexpressor strains 4R and 7R. When APC from E-expressor strains were used and alloreactivity against the incompatible E molecules was removed by BUdR + light treatment, 7R T cells responded to GLT presented by 9R APC, but 4R T cells failed to respond to GLT presented by 2R APC. However, 4R T cells mounted a proliferative response to GLT presented by fully allogeneic 5R or 9R APC. The latter response was completely abolished by the depletion of cells alloreactive against 2R and 5R or 2R and 9R. Since removal of alloreactivity against 5R plus 9R did not affect the response of 4R T cells to GLT presented by either 5R or 9R cells, we conclude that the 4R T cells generated in response to GLT cross-react with the additional incompatibility presented by 2R cells, that is, the Ek beta chain. In contrast, 7R T cells recognizing GLT presented by 9R APC do not cross-react with Ek beta. These results demonstrate that "blind spots" in the T cell repertoire produced by depletion of cells alloreactive against a ***single*** ***chain*** of a class II MHC molecule can render a strain nonresponsive to a synthetic polypeptide antigen, and that this nonresponsiveness corresponds to that attributed to the MHC-linked Ir genes.

=> log y
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	57.24	57.45

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